THE PAST, PRESENT AND AN OUTLOOK ON THE FUTURE OF EVIDENCE DEVELOPMENT FOR DIGITAL THERAPEUTICS

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SUMMARY

- Evidence generation supporting the value of digital therapeutic (DTx) has been haphazard, with some manufacturers opting for using data collected through randomized clinical trials (RCTs), while others utilize Real World Evidence (RWE)
- While guidance on appropriate endpoint selection has been scarce, manufacturers have consistently used functional and engagement endpoints in their studies
- Existing evidence and evaluation frameworks are not always well equipped to demonstrate the value of DTx; as a result, new methods of data collection and value demonstration may be needed

INTRODUCTION

- Digital Therapeutics (DTx) are medical interventions offered directly to patients using evidence-based, clinically evaluated software to treat, manage, and prevent a broad spectrum of diseases and disorders[1]
- While there has been an increase in the number of DTx solutions that have been introduced to the market, their reimbursement and adoption are scarce[1,5]
- Randomized clinical trials are a source of DTx evidence, similar to pharmaceuticals or medical devices[6]. In addition, the use of real-world evidence (RWE) has been increasingly explored for DTx value demonstration[2,4]
- The robustness of RWE, and the lack of standardization in the evidence submitted, have historically been a source of concern for DTx, impairing the ability to receive regulatory approval and be reimbursed by payer bodies[2,3]
- As the quantity of DTx expected to enter the market in the next few years increases, it is imperative to gain further understanding of the evidence requirements for DTx and reach alignment across relevant organizations on the appropriate framework for the evaluation of DTx across therapeutic areas and product types

OBJECTIVES

- This study aims to understand the current trends in evidence generation for DTx, and to evaluate how this may impact the assessment of these therapies
- The analysis will describe the strength and influence that different types of evidence and endpoints have had in the value assessment, coverage, reimbursement, and adoption of DTx

METHODS

- A targeted literature review was conducted to understand the evidence generated and submitted as a part of DTx commercialization
- The research team identified key topics of interest from an academic and industry perspective by utilizing PubMed, ISPOR, and Clinicaltrials.gov databases and carried out targeted hand searches to gather industry-generated resources that covered the evidence requirements for DTx and expectations from payers
- The PubMed search strategy (Table 1) focused on identifying the key study types utilized in the peer-reviewed DTx publications over the last 5 years; the search strategy retrieved 226 abstracts
- To identify the current endpoints used in randomized clinical trials (RCTs) for DTx, a subsequent search strategy was generated in Clinicaltrials.gov (Table 2), which retrieved 71 results; additionally, the ISPOR database (Table 3) was explored (retrieved 347 results) to assess key topics/areas of discussion within the HEOR community around DTx

Table 1 | PubMed Search Strategy

Digital Therapeutic Terms	"Digital Therapeutic*"[Title/Abstract] AND "study"[Title/Abstract]
Filters	2018-2023
Relevant Results (N)	180 publications

Table 2 | ClinicalTrials.gov Search Strategy

Search Terms	"Digital Therapeutic"
Filters	2018-2023; Industry/Other Sponsored; Completed Trials
Relevant Results (N)	25 studies

Table 3 | ISPOR Database Search Strategy

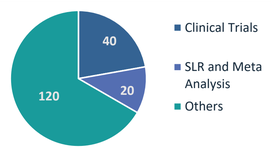
Search Terms	"Digital Therapeutic" OR "Digital Therapeutics" OR "DTX" OR "DTx"
Filters	Across study types
Relevant Results (N)	104 presentations

RESULTS

Figure 1 |Study Type

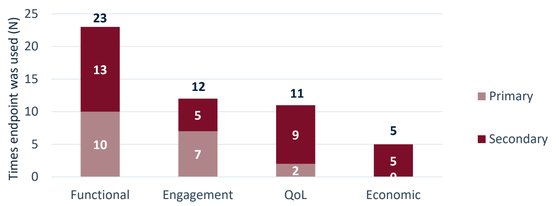
- Multiple study types have been used to date to assess the value of DTx; the largest category of study types is covered under the "Others" category, which includes retrospective studies including electronic health records and registry data (50%), feasibility studies (20%), program implementation studies (20%) and qualitative interviews (10%)

Key Finding: The use of randomized controlled trials to justify the value of DTx is uncommon, with ~20% of products having data generated through this study type



Figures 2 and 3 |Common Primary and Secondary Endpoints

- When assessing the completed clinical trials that justify the value of DTx, the primary and secondary endpoints used can be split into four categories[7-14]:
- *Domain 1 (Engagement): Patient use of the app/adherence over time*
- *Domain 2 (Functional Endpoint): Disease-specific endpoints that justify the value of the DTx in terms of patient-relevant outcomes*
- *Domain 3 (Quality of life [QoL]): General or disease-specific QoL scales*
- *Domain 4 (Economic impact): Measurement of the reduction of the use of prior SoC, reduction in the number of hospital visits/physician time, ability to work*



Key Finding: Functional endpoints are most used as primary or secondary value metrics in RCTs; the use of economic endpoints is limited, and commonly included as a secondary value metric

DOMAIN 1 ENGAGEMENT

DOMAIN 2 FUNCTIONAL ENDPOINT

DOMAIN 3 QoL

DOMAIN 4 ECONOMIC IMPACT

DISCUSSION & CONCLUSION

Discussion:

- The adoption and reimbursement of DTx have faced significant challenges to date due to system-level concerns around their clinical and economic value demonstration given the lack of understanding on the most appropriate frameworks for their assessment
  - For example, Pear Therapeutics, the company at the forefront of DTx development, focused their evidence generation plans on real-world observational evaluation vs. clinical trials and generating data around patient engagement and retention; while Pear's products have demonstrated to be clinically valuable and provide cost savings, concerns around the value of their products remained across payer organizations
  - Another example is, Sleepio, Big Health's insomnia DTx, which generated evidence through RCTs; Big Health focused on specific subpopulations with a high unmet need, and used functional endpoints to demonstrate product value (e.g., change in insomnia severity index scale, QoL), while their approach led to positive feedback from payers and providers alike, Sleepio is not extensive covered by payer organizations
- While the use of RCTs that include functional endpoints have resonated the most with payer bodies (i.e., BigHealth's Sleepio), the drivers of DTx reimbursement remain unknown, as DTx products have yet to achieve extensive coverage and availability
- As the number of DTx in the market increases over the next 2-3 years, it would be beneficial to create a unified framework for the evaluation of DTx, while aligning on evidence requirements; further exploration into the value of RWE to demonstrate the value of DTx, and the definition of the appropriate assessment domains for DTx is needed

Conclusion:

- This research reviews the evidence requirements for DTx, the endpoints required, and assesses the impact of RWE to support the clinical and economical value of DTx. While there seems to be a strong preference for RCTs collecting data through functional endpoints, uncertainties remain around the most appropriate study type to justify the value of DTx and enable extensive reimbursement across payer organizations

Future Research Opportunities:

- This research is foundational in understanding the evidence generated to date to justify the value of DTx; however, the research focused on trials that have been completed, excluding ongoing studies that might influence future trends in the DTx evidence generation space
- Future research should further investigate the assessment frameworks published by relevant organizations, and understand the payer perspective around the evidence required to support reimbursement of DTx (including study type, durations, and comparator selection)

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